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CERTAIN ASPECTS OF HUMAN METABOLISM DURING SPACEFLIGHTS OF VARYING DURATION

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Translation of "Nekotoryye storony obmena veshchestv cheloveka v kosmicheskikh poletakh razlichnoy prodolzhitel'nosti". 1st Meeting of the Joint Soviet-American Working Group on Space Biology and Medicine, 1987, Nal'chik, USSR, 2-11 August 1987.

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16. Abstract

A comparative analysis is made of hormone reactions after short term and long term dpaceflights. Endorinological indicators of the venous blood and daily urine of cosmonauts completing flights lasting from 7 to 237 days were examined. It was found that there is no pathological direction in the metabolic shifts in the erythrocytes and disruption of the functional state of their membranes.

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CERTAIN ASPECTS OF HUMAN METABOLISM DURING SPACEFLIGHTS OF VARYING DURATION

A. NEUROHUMORAL REGULATION

Studies on hormone reactions in a person during a spaceflight are few in number (Leach, 1981; Kvetyanski, 1987). A similar endocrinological examination of cosmonauts is usually conducted after a flight (Leach, 1981; Kvetnyanski, 1987; Tigranyan et al., 1984; Kalita, Tigranyan, 1986; Afonin et al., 1986; Ushakov et al., 1986; Tigranyan et al., 1987). However, it is difficult to judge the special features of hormone control under weightlessness conditions based on these data. The individual nature of the hormone responses is significantly pronounced and hinders the superpositioning of various, frequently directly contradictory, effects, among which are the residual effect of weightlessness, the effect of overloads in the concluding stage of a spaceflight, the rediscovered effect of the Earth's gravitational factor and other forms of stress.

It is possible to expect that, with all other characteristics of any active factor being equal, its effect on the functional systems will depend on their initial condition. This means that the condition, in which the hormone systems are in weightlessness, will be reflected to a significant degree in their responses to the action of a set of factors associated with the completion of the spaceflight.

The regulation systems' functional state will obviously be different during short-term and long-term adaptation to the effect of weightlessness. In connection with this, the necessity arises of conducting a comparative

analysis of hormone reactions after short-term and long-term spaceflights. At the same time, one of the important questions, which is to be discussed in this report, is the evaluation of the adequacy of the target cells' response reaction to the blood's hormone content after spaceflights of varying duration.

The endocrinological indicators of the venous blood and daily urine of cosmonauts who have completed flights lasting from 7 to 237 days have been examined. Biochemical analyses of the blood were conducted twice before the flight and also on the 1st and 7th days after the flight. The daily urine was collected over the course of three days successively 30 days and 5 days before the launching, on the landing day and over the course of the first 10 days of the post-flight period. Blood samples were taken in the morning on an empty stomach in a reclining position from the ulnar vein.

The concentrations of epinephrine (E) [A — adrenalin] and norepinephrine (NE) [NA — noradrenalin] in the blood plasma or serum were determined using the fluorometric method and the concentrations of 3,5,-cyclo-AMP (cAMP) [AMF — adenozinmonofosfat, AMP — adenosine monophosphate], 3,5,-cyclo-GMP (cGMP) [GMF — guanozinmonopfosfat, GMP — guanosine monophosphate], prostaglandins, STH [STG — somatotropnyy gormon, STH — somatotropic hormone], TTH [TTG — tireotropnyy gormon, TTH — thyrotropic hormone], ACTH [AKTG — adrenokortikotropnyy gormon, ACTH — adrenocorticotropic hormone], cortisol, aldosterone, the activity of plasma renin, insulin, triiodothyronine, thyroxine, and testosterone by the RIA method [expasion uncertain]. The urine was tested for E, NE, dopamine and DOPA [DOFA — dioksifenilalanin, DOPA — dihydroxyphenylalanine] using the

fluorometric method, catecholamine-metabolism products (CA) [KA — katekholamin] — metanephrine (MN) [MN — metanefrin], normetanephrine (NMN) [NMN — normetanefrin], vanillylmandelic acid (VMA) [VMK — vanililmindl'naya kislota] and homovanillic acid (HVA) [GVK — gomovanilinovaya kislota] — using the thin-layer chromatography method and aldosterone using the RIA method.

During the period of the 237-day space mission, on the 216th through the 219th days of the flight, venous blood was taken from all the crew members using the "Plazma-01" [plasma] system and the daily urine was collected, the specimens of which were sent to a laboratory for subsequent analysis. The schematic depiction of the sequential operations using the Plazma-01 system is presented in figure 1. The concentrations in the blood and urine specimens of aldosterone, cortisol, desoxycortisol, desoxycorticosterone, the antidiuretic hormone and the activity of the plasma renin were determined using the RIA method. 13

The mathematical processing of the data was conducted using the variational statistics method.

The use of the analysis of single-factor variance with the null hypothesis regarding the equality of averages and the variance for groups with a varying number of observations indicated the presence of significant differences for a number of biochemical parameters only between the groups of cosmonauts who completed the short-term (up to 14 days) flights and those who completed the longer-term flights. No significant difference for the majority of biochemical indicators was discovered between the groups whose flights lasted from 60 to 237 days, which, evidently, points to a specific

stabilization of the adaptation process after a two-month stay in weightlessness. This produces a basis for dividing the flights based on the duration principle into two groups: short-term (up to 14 days) and long-term (beginning with the 60th day), and for conducting their comparative analysis.

Activation of the sympathoadrenal system (SAS) [SAS — simpato-adrenalovaya sistema] was observed after all the space missions to the Soviet Salyut orbital scientific research complex. This was manifested by an increase in the CA concentration in the blood and an increase in the urinary excretion of E, NE, dopamine, DOPA and CA-metabolism products. The results of the studies have been described in detail in preceding works (Davydova and Tigranyan, 1982; Davydova et al., 1984).

It is important to note that the concentration of E in the blood was substantially higher after long-term flights than after short-term ones (figure 2). At the same time, the ratio of E/NE as an indirect indicator of the relative activity of the hormone and mediator components of the SAS increased substantially only after long-term flights. The following differences in the urinary excretion of CA and their metabolites are typical for the first few days after the completion of space flights of varying duration (figure 3). The excretion of E in contrast to NE increased to a greater degree after a long-term stay in weightlessness, while the urinary excretion of O-methylation products (MN, NMN) (figure 4) and those of CA-oxidation deamination (VMA, HVA) (figure 5) increased only after short-term missions. The differences in the SAS reaction after short-term and long-term flights were uncovered also during calculation of the relative activity indicators of the CA-metabolism tracts and it all comes down to two basic

points. After a long-term stay in weightlessness, the proportion of E, entering the urine primarily from the adrenal glands, and NE, excreted basically by the sympathetic nerve endings, is substantially higher. This indirectly testifies to the stronger and more persistent activation of the SAS' hormone component. Moreover, a protractedly maintained (up to 10 days) increase in the ratio of excreted VMA to the total urinary excretion of O-methylated CA-metabolism products is observed after long-term space missions. If the VMA is considered to be the basic metabolite of E and NE for the O-methylation and the oxidation deamination pathways, then these data point to a primary inactivation of the CA circulating in the blood in oxidation deamination reactions.

The results of the studies of the SAS' activity on the 217th through the 219th day of the long-term flight testify to its insignificant changes (there was a certain increase in the CA concentration in the blood plasma in all the crew members and a maintaining of their urinary excretion level in comparison with the background values). These data support the established notion regarding the lack of SAS activation during long-term spaceflights, which is in keeping with the data of American researchers who conducted similar studies on board the Skylab orbital station.

The hormone reactions of the pituitary-adrenal system also differed after short-term and long-term spaceflights. Despite the lack of significant changes in the concentration of pituitary hormones in the blood after both a short-term and a long-term stay in weightlessness, the glucocorticoid and mineralocorticoid responses of the adrenal glands were significantly greater after short-term flights, when a substantial increase in the concentration of

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cortisol and aldosterone in the blood was noted (figure 6). In conformity with the increased level of aldosterone in the blood after short spaceflights, also observed were an increase in the plasma renin activity and an intensification of urinary excretion of aldosterone (figure 7). In contrast to this, after a long-term stay in weightlessness, instead of an increase, a decrease in plasma renin activity and the aldosterone concentration in the blood was observed, although its renal excretion increased during the first 7 days after the flight. Along with this, only after long-term spaceflights was a decrease noted in the testosterone concentration in the blood.

The studies conducted during the flight on the 217th through the 219th days indicated that aldosterone excretion during this period increased. Simultaneously, there was a decrease in 2-DOC [DOK — dezoksikortikosteron, DOC — desoxycorticosterone] excretion and particularly the fraction of glupuronides, which are predecessors of aldosterone, which testifies to its mobilization for synthesis of the basic mineralocorticoid. At the same time, the aldosterone content in the blood plasma changed insignificantly, while the renin concentration increased. The cortisol concentration in the blood plasma increased in comparison with the background values. These data testify to the fact that, during the study period (from the 217th to the 219th day of the flight), there occurred activation of the mineralocorticoid and glucocorticoid functions of the adrenal glands. During this same period, an increase was noted in the urinary ADH [ADG — antidiureticheskiy gormon, ADH — antidiuretic hormone] excretion against the background of its tendency to decrease in the blood (figures 8, 9 and 9a).

Substantial differences between the groups of cosmonauts, who were in

weightlessness for a short time and a long time, were also observed in the reactions of the thyroid gland and the tissue hormones (figure 10). Only after long-term flights was a significant increase discovered in the thyroxine concentration in the blood. At the same time, the long-term flights did not lead to changes in the cAMP level in the blood to the same pronounced degree as is typical for short-term flights. The reaction of the systems which ensure the presence of prostaglandins in the blood did not depend on the length of the stay in weightlessness and lead to a lowering of their concentration in the blood after the flight. But in this instance, the level of pressor prostaglandins (G_2) decreased to a large degree after long-term flights, while after short-term flights, that of the depressor prostaglandins (A+E) decreased.

Regardless of the length of the flight, the insulin concentration in the cosmonauts changed during the post-flight period. And, in both instances, a sharp increase in the blood insulin level was noted after flight and was maintained even on the 7th day of the re-adaptation period (figure 11).

The analysis conducted on the obtained data indicated that the cosmonauts' hormone reactions after the completion of the flights differed substantially in relation to the length of the stay in weightlessness. After long-term flights, in comparison with the short-term ones, a more pronounced persistent activation of the SAS was observed. A typical feature of CA metabolism during the re-adaptation period after long-term flights is the intensification of CA inactivation primarily by means of their oxidation deamination with a simultaneous decrease in the production of methylated E and NE metabolism products.

The hormone reactions of the pituitary-adrenal system after short-term and long-term spaceflights also differ. Based on the cited data, it is possible to assume that, a after short-term stay in weightlessness, the specific homeostatic reactions are limited by a moderate activation of the SAS and an adequate reaction of the systems which implement the tissue effects of the CA. Among such systems are the prostaglandins, the adenyl cyclase system and the renin-angiotensin-aldosterone system. In order to judge the adequacy of the reactions, it is important to trace how the activity of these systems changes after a flight.

The interaction of catecholamines with β-adrenergic receptors leads to the activation of the adenyl cyclase and the formation of cAMP. The increase in the blood concentration of this product was observed only after short-term spaceflights. In the first few days after landing, the concentration of A+E prostaglandins was significantly reduced, which can be considered as an adequate response of the tissue mechanisms which regulate the vessel tone to the increase in pressor action caused by adrenergic stimulation. Not excluded, however, is the fact that the decrease in the depressor prostagladin concentration in the blood is determined not only by changes in the regulation system for the vasomotor reactions, but also reflects changes in other aspects of the tissue metabolism, such as, for example, the water-salt exchange.

In the first few days after the landing, a decrease was noted in the majority of cosmonauts in diuresis and the excretion of sodium, potassium and osmotically active substances (Grigor'yev et al., 198?). Regardless of the length of the flights, the authors discovered in practically all the

cosmonauts after landing a disparity between the osmolarity of the urine and the magnitude of the diuresis. This was expressed by the fact that, immediately after landing, against the background of the decreased amount of diuresis, the osmotic concentration of the urine did not increase, like under the usual physiological conditions, rather, it decreased. At the same time, the ADH concentration in the blood was higher than before the flight, i.e., an inadequate reaction of the renal receptors to the hormone was uncovered.

Along with the activation of the antidiuretic system in the first few days after the end of short-term flights, there occurred a substantial increase in plasma renin activity, in the aldosterone concentration in the blood and an intensification of its urinary excretion. It is obvious that the increase in the aldosterone content in the blood was caused by the increase in plasma renin activity.

In the first few days after the completion of long-term spaceflights, despite the significant activation of the SAS, the concentration of pituitary hormones, cortisol, cAMP and depressor prostaglandins in the blood, for all practical purposes, did not differ from the pre-flight level. At the same time, the concentration of aldosterone, testosterone and pressor prostaglandins and the plasma renin activity were even lower than before the flight. The impression is formed that long-term flights require less stress on the neurohumoral regulation systems than short-term ones. However, this is contradicted by the data from clinical physiological examinations of the cosmonauts. It must be assumed, therefore, that a qualitatively different reaction took place after the long-term flights.

First of all, the significant activation of the SAS' hormone component

attracts our attention. Under normal conditions, the changes in such a direction, even with a lesser degree of pronouncement, lead to the activation of the β-adrenergic receptors, accompanied by an increase in the tissues, and then in the blood also, of the cAMP concentration and an increase in the ratio of cyclic adenyl nucleotides to guanil ones, which was also noted after short-term spaceflights. After long-term flights, the cAMP content in the blood did not change and the ratio of cAMP/cGMP even decreased, i.e., despite the high level of epinephrine in the blood, the action of the mediator on the β-adrenoreceptors of the target cells did not intensify, which makes it possible to assume a certain functional blocking of adrenoreception. These data once again are proof of the necessity of studying not only the concentration of hormones in the blood, but also what is, in all probability, more important, the state of the tissue receptors of the target organs.

Also proof of the decrease in the reactivity of the adrenergic receptors are the data obtained during the study of the special features of catecholamine metabolism. The intensification of the inactivation of the catecholamines is accompanied by a decrease in the production of methylated metabolism products of epinephrine and norepinephrine, i.e., the active excretion of catecholamines until they manifest their own physiological action.

An alternative reason for the decrease in adrenoreactivity may be the overall decrease in the level of functional activity which occurs in weightlessness. The data obtained during the flights for the Skylab program indicated that the urinary excretion of norepinephrine decreased during the flight (Leach. 1981). The necessity arose of determining the catecholamines

in the blood during a flight, which was accomplished in the joint Soviet-Czechoslovakian studies during the 237-day spaceflight (Kvetnyanski, 1987). The obtained data indicated that, under the conditions of weightlessness, the level of the catecholamines in the blood, for all practical purposes, did not differ from the pre-flight level, while the metabolism of the catecholamines and the products of their oxidation deamination decreased. If it is assumed that the restructuring of the SAS occurs in weightlessness and is adaptive for these conditions, then the secretion capability of the system is maintained, changing rapidly depending on the conditions of the re-adaptation period, while the state of its receptor component is conservative and is maintained for a longer period of time after the end of the flight.

Also testifying to the decrease in tissue reactivity in relation to the catecholamines are the inadequate reactions of the renin-angiotensin system in response to the significant activation of the SAS' hormone component after long-term flights. Inasmuch as the sympathoadrenal mechanisms with the participation of the adrenergic receptors have a determining significance in the activation of renin secretion in a person, the decrease in the functional [text unreadable here] plasma renin [activity], which determines the low concentration of aldosterone in the blood. Under the conditions of an acute re-adaptation period, when water and electrolyte retention occurs in the body, the low level of aldosterone in the blood hinders the normalization process for water-salt homeostasis. /10

When the regulator systems are functioning normally, the SAS' increased activity through the adrenergic mechanisms retards the glucose-dependent

secretion of insulin. After spaceflights, regardless of their length, a significant increase in the insulin concentration in the blood was observed. This is yet another fact in favor of the assumed decrease in tissue adrenoreactivity. The specific resistance of the pancreas' receptor mechanism to a hormone, in contrast to other target organs, appears even after a short-term stay in weightlessness. The same can also be said about the hormone-receptor interaction of ADH and the kidney as the target organ.

One of the key regulators of cellular energy formation is thyroxine. An increase in the concentration of this hormone in the blood was observed only after long-term flights. The thyroid hormones in a person increase the consumption of oxygen and stimulate and accelerate the oxidation metabolism of proteins, fats and carbohydrates. During a flight, the oxygen consumption is substantially reduced (Leach, 1981). Also decreased by 40% is the partial pressure of oxygen in the peripheral tissues and its local use (Haase et al., 1986). These data do not produce any basis for associating the post-flight activation of the thyroid gland with the direct action of spaceflight factors. It is more likely that the stimulation of the thyroid gland's endocrine function occurs not in weightlessness, but rather, in the acute re-adaptation period and is aimed at an urgent intensification of energy production.

Thus, the functional restructuring of the hormone regulation system under the action of spaceflight factors has its own special features in relation to the length of the flight. The interaction of the various hormone systems does not undergo large changes during the adaptation to a short-term stay in weightlessness. After flights lasting up to 14 days, a moderate activation of the sympathoadrenal system arises, the effects of which basically are

adequately transmitted to the receptor structures of the target cells and are realized by the tissues. In contrast to this, long-term spaceflights cause changes in the homeostatic reactions, which make it possible to assume a decrease in the functional activity of the receptor structures.

B. SPECIAL FEATURES OF HUMAN ERYTHROCYTE METABOLISM UNDER LONG-TERM SPACEFLIGHT CONDITIONS.

Studies on the effect of long-term weightlessness on the metabolism of red blood corpuscles, conducted earlier, made it possible to uncover certain shifts in the energy-producing metabolism of erythrocytes. One of these shifts is the decrease in the ATP concentration against the background of a normal or enhanced glycolytic process. At the same time, after the completion of the 63- and 140- day flights, a tendency toward a decrease in ATP with a simultaneous decrease in glycolytic activity was noted, which, in all probability, reflected the functional state of the entire body, which was characterized by a reduced energy-producing metabolism under the flight conditions. The uncovered decrease in the ATP level with the simultaneous intensification of the energy-producing process may testify to an increase in the rate of ATP-consuming processes, in particular, to the intensification of transport ATP-ase in connection with the possible shifts at the membrane level. Moreover, not excluded is the possibility of a decrease in the pool of nucleotides, caused by the overall catabolic direction of the processes in the body. In connection with the above-stated item, an extensive study was undertaken, in which, along with the previously studied indicators of

metabolism in erythrocytes (the content of ATP and 2,3-diphosphoglycerate (2,3-DPG) [DFG — difosfoglitserat], the intensity of the glycolysis, the level of the reduced glutathione (QSH), the activity of the lactate dehydrogenase (LDH) [LDG — lactatdegidrogenaza] and glucose-6-phosphate dehydrogenase (G-6-PD) [G-6-FD — glyukozo-6-fosfatdegidrogenaza]) a determination was made of such parameters as the rate of glucose consumption, which characterizes the intensity of the pathways which are basic in erythrocytes (Embden-Meyerhof and pentose phosphate), the content of the oxidized form of glutathione (GSSG) and glucose-6-phosphate (G-6-P) — the initial substrate of the pentose phosphate pathway, the latter is responsible for the oxidation-reduction reactions in the cell, the permeability of the erythrocyte membrane (for the escape of K^+ into the external medium), the sensitivity of the cell to the oxidizing and mechanical actions, the intensity of the processes of lipid peroxidation (LP) [POL — perekisnoye okisleniye lipidov] and the spectrum of fatty acids — indicators which characterize the condition of the membrane.

For the purpose of determining these indicators, the cosmonauts were examined before and after completion of flights on board the Salyut-7 orbital station.

As a result of the study of the indicators for the energy-producing processes in erythrocytes, a tendency toward a decrease in its intensity in the first few days after the completion of a spaceflight was uncovered. This tendency was manifested in a decrease in the glucose consumption rate ($V_{gluc.}$), which was discovered in one of the cosmonauts, and also in a certain decrease in the growth of lactate ($V_{gluc.}$) during the incubation of

erythrocytes in plasma and in a physiological solution. At the same time, a decrease was noted in the concentration of ATP in both the samples, fixed immediately after the taking of the blood and also the incubation period of the erythrocyte suspension (table 12).

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During the study of the pentose phosphate pathway for the glucose oxidation, the basic role of which consisted of maintaining the oxidation-reduction processes in the cell, changes were discovered which were expressed in the decrease in the G-6-P content (figure 13). This may be caused by the increase in its oxidation in the pentose phosphate pathway. What speaks in favor of this assumption is the intensification discovered by us of the activity of the G-6-PD. These changes, in all probability, were aimed at maintaining the oxidation-reduction processes in the cell and, first of all, the content of reduced glutathione, the concentration of which had been reduced, particularly in the first days after landing, which, probably, can be explained by the decrease in its (GSH) synthesis. This is testified to by the data obtained during the determination of the stock of free amino acids in the plasma, which point to a catabolic direction for the processes in the body after the long-term action of weightlessness. Moreover, not excluded is the possibility of a decrease in the reduced glutathione content due to a certain strengthening of the intensity of the oxidizing processes. This is pointed to by the increase in the concentration of oxidized glutathione during the incubation of the erythrocyte suspension in the plasma and the fraction. The increase in this indicator was particularly pronounced in cosmonaut 1 on the 7th day after landing. At the same time, a certain activation of the oxidation processes is not substantial and does not cause disruptions in the

cells' stability. This is supported by the data obtained during the study of the membranes' functional state (figure 14) which testify to the fact that the effect of the oxidation stress (the introduction into the sample of tretbutylhydroperoxide) die not cause substantial shifts in the level of oxidized glutathione in comparison with the physiological norm.

During the measuring of the rate of K^+-escape into the external medium, no differences were discovered in both cosmonauts in comparison with the studies and the physiological norm. This testifies to the lack of disruptions in the permeability of the erythrocyte membrane. The study of the rate of hemolysis with the effect of a mechanical load also did not uncover substantial shifts during the study of the specific resistance of the cosmonauts' and donors' erythrocytes. Also testifying to the lack of significant activation of the oxidation processes in the erythrocytes are the data about the state of the LP in the erythrocyte membranes (table 15). Thus, in the first days after a flight, a decrease was noted in the content of hydroperoxides and secondary LP products. At the same time, a notable decrease was discovered in both cosmonauts in the content of polyunsaturated fatty acids — a decrease in linolic acid ($C_{18:2}$) and a lack of eicosatrienic ($C_{20:3}$) and arachidonic ($C_{20:4}$) acids. The increase in the content of polyunsaturated fatty acids on the 7th day after the flight was accompanied by an increase in the lipid peroxidation processes and, at the same time, a certain increase was noted in the content of hydroperoxides, as was a simultaneous increase in the level of secondary products by a factor of 2.

Thus, the obtained results, which are of a preliminary nature because of their paucity, testify to the lack of a pathological direction in the observed

metabolic shifts in the erythrocytes and the disruption of the functional state of their membranes. The noted changes in the indicators for the metabolism of the erythrocytes are, to all appearances, of an adaptation nature and are caused by regulator reactions aimed at maintaining the structural and functional integrity of the cell.

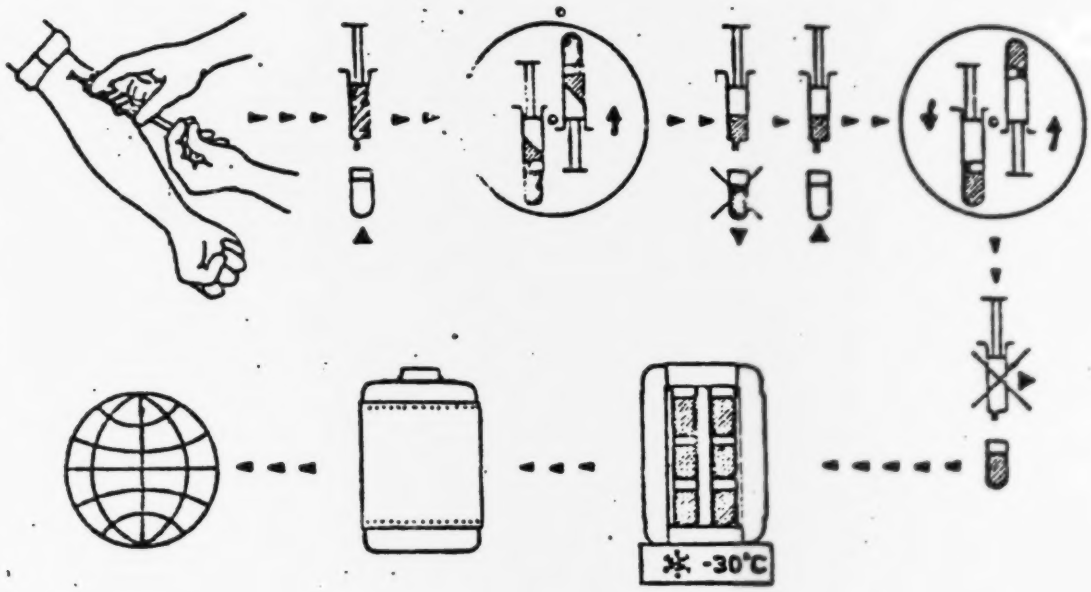

Fig. 1 Schematic presentation of the individual steps in using the appliance "Plasma 01"

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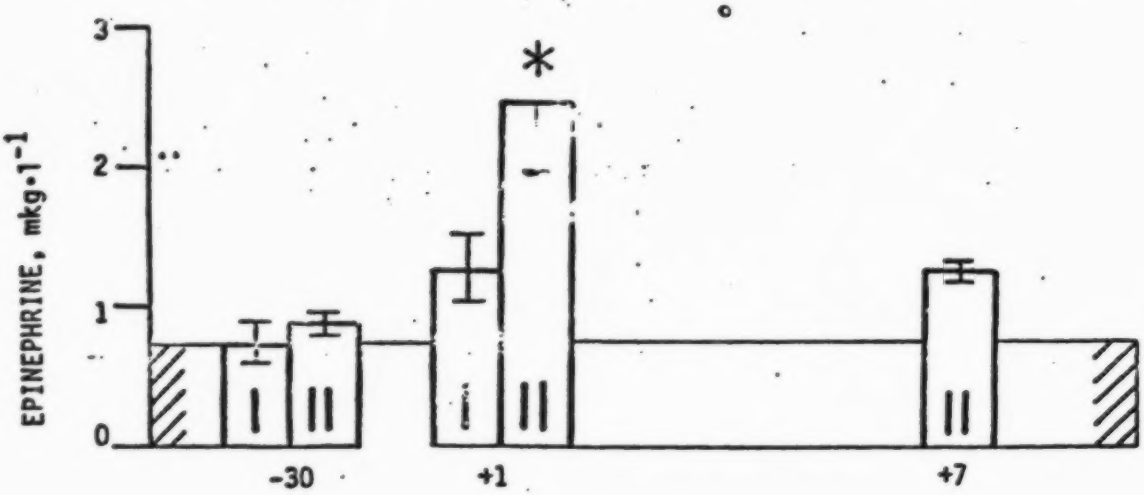
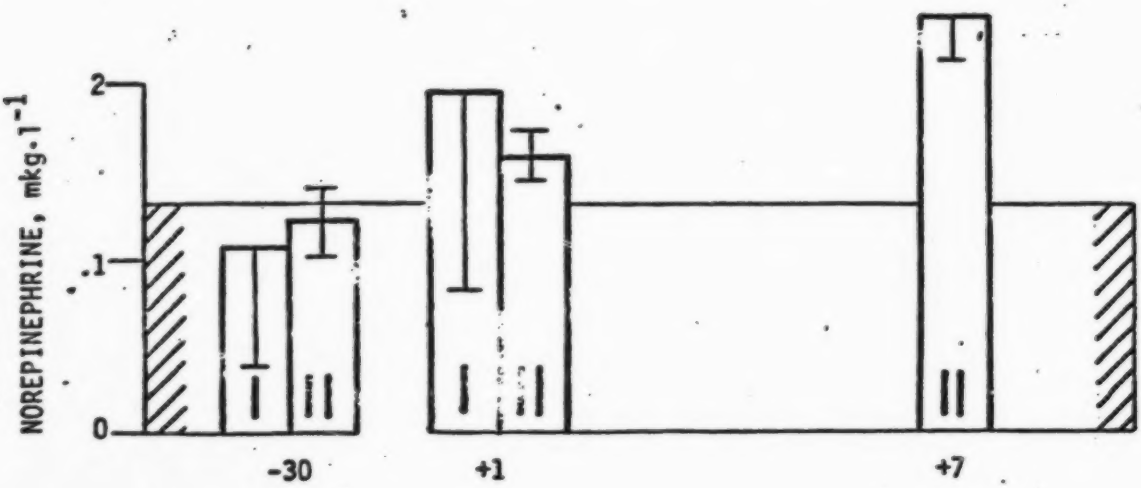
PLASMA CONCENTRATION OF EPINEPHRINE (E), NOREPINEPHRINE (NE) AND RELATION E/NE AFTER SHORT-TERM (I,n=17) AND LONG-TERM (II,n=13) SPACE FLIGHTS





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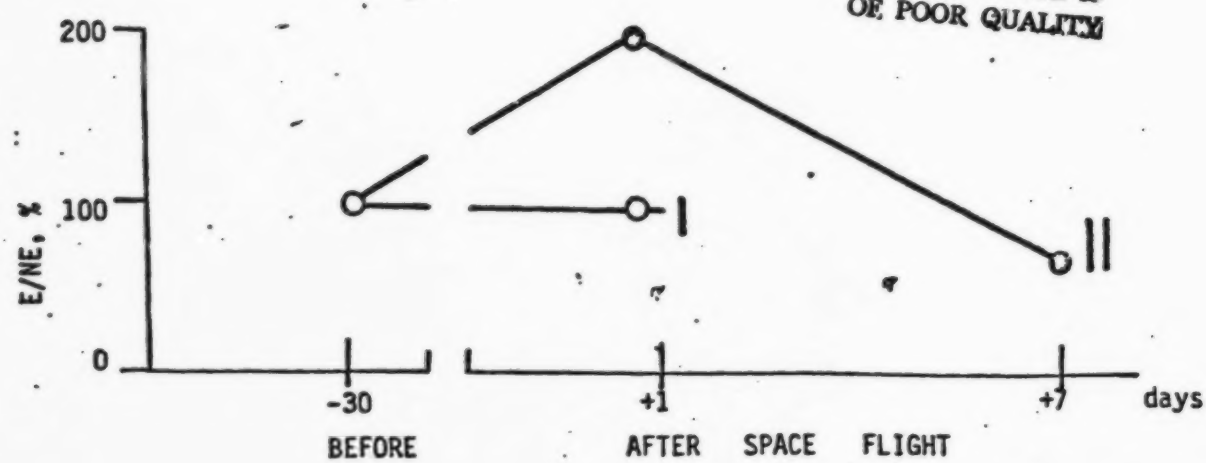
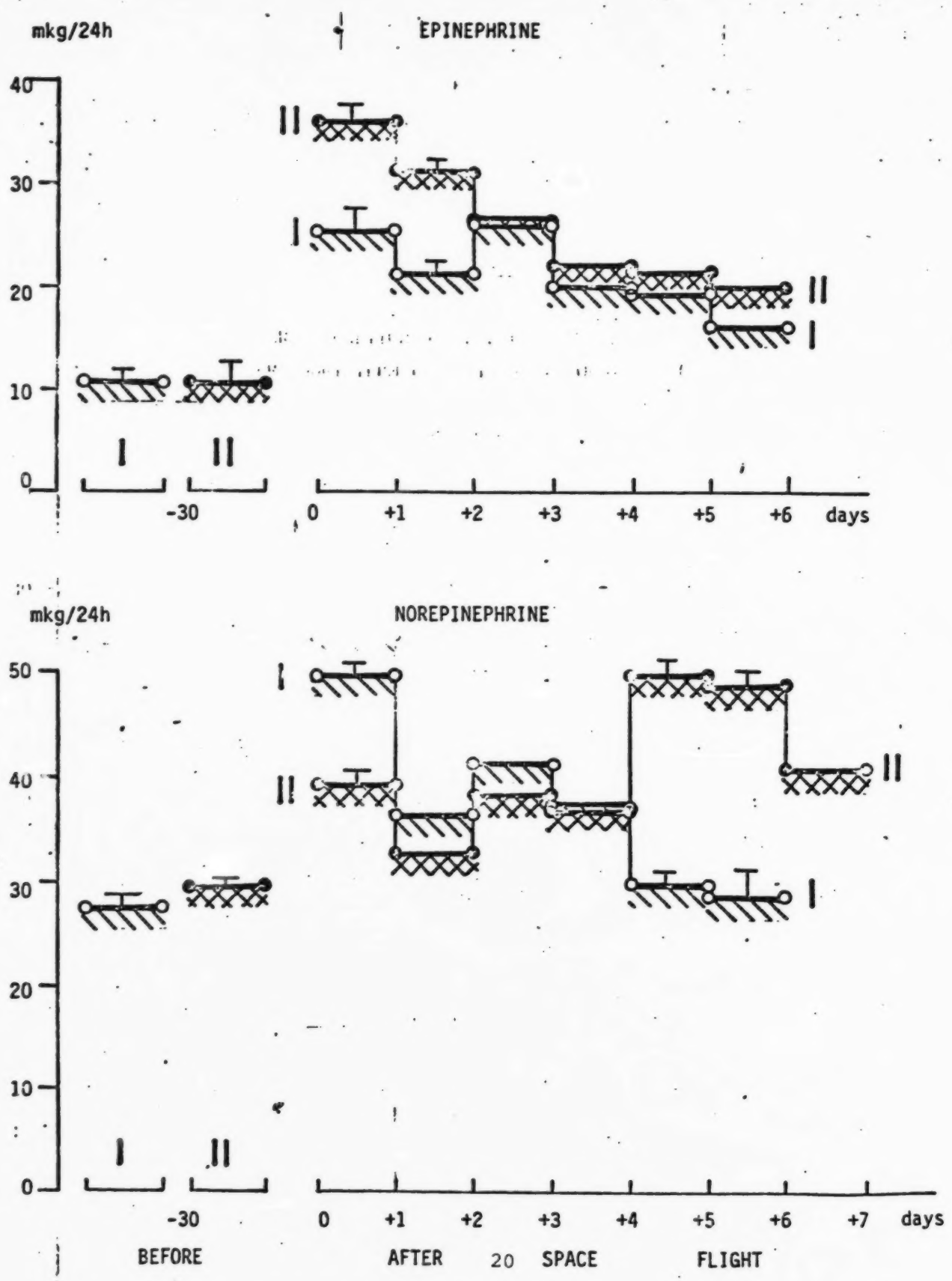
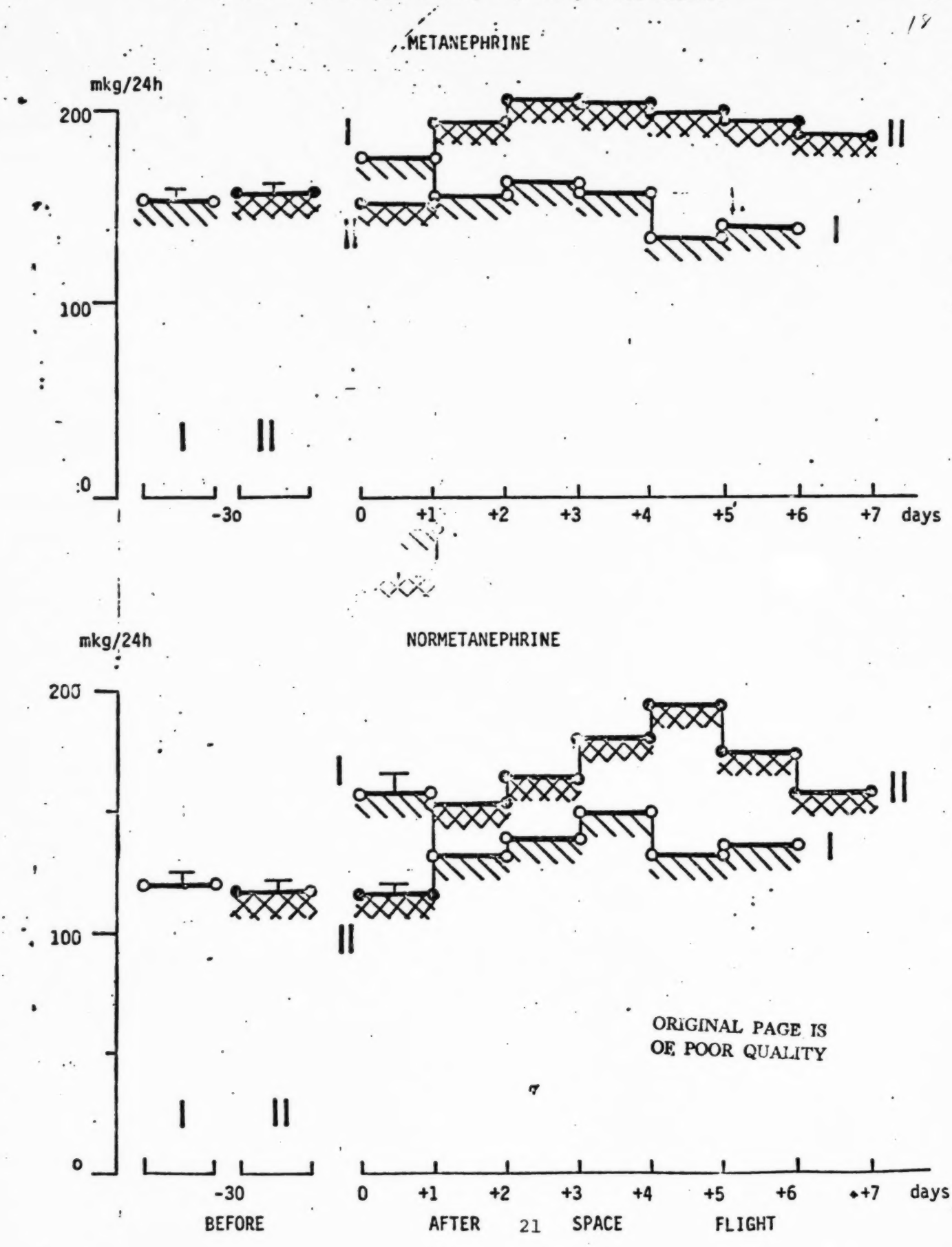


URINARY EXCRETION OF FREE EPINEPHRINE AND NOREPINEPHRINE /9
AFTER SHORT-TERM (I,n=17)AND LONG-TERM (II,n=13) SPACE FLIGHTS



(I,n=17) AND LONG-TERM (II,n=13) SPACE FLIGHTS



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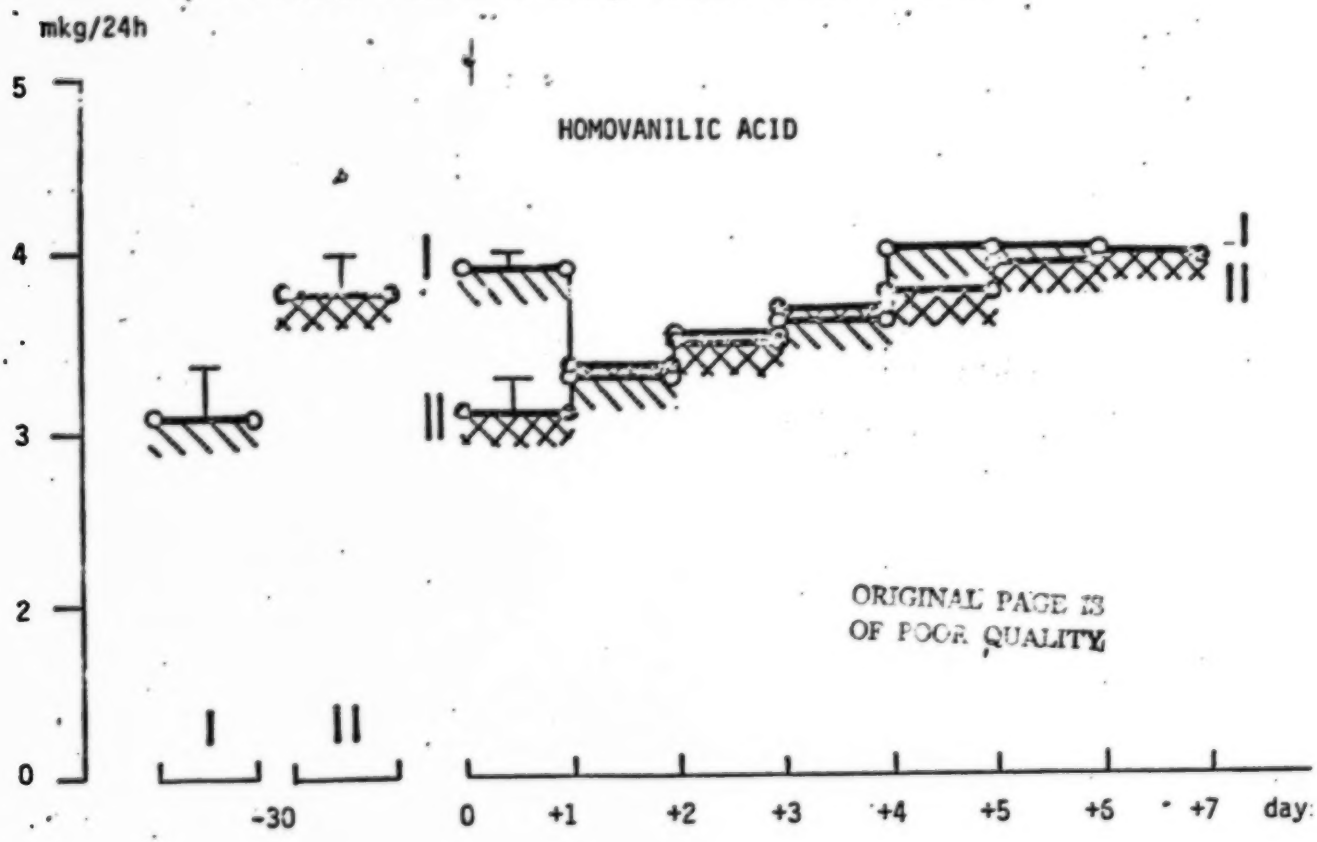
URINARY EXCRETOIN OF CATECHOLAMINE METABOLITES AFTER SHORT-TERM (I,n=17) AND LONG-TERM (II,n=13) SPACE FLIGHTS



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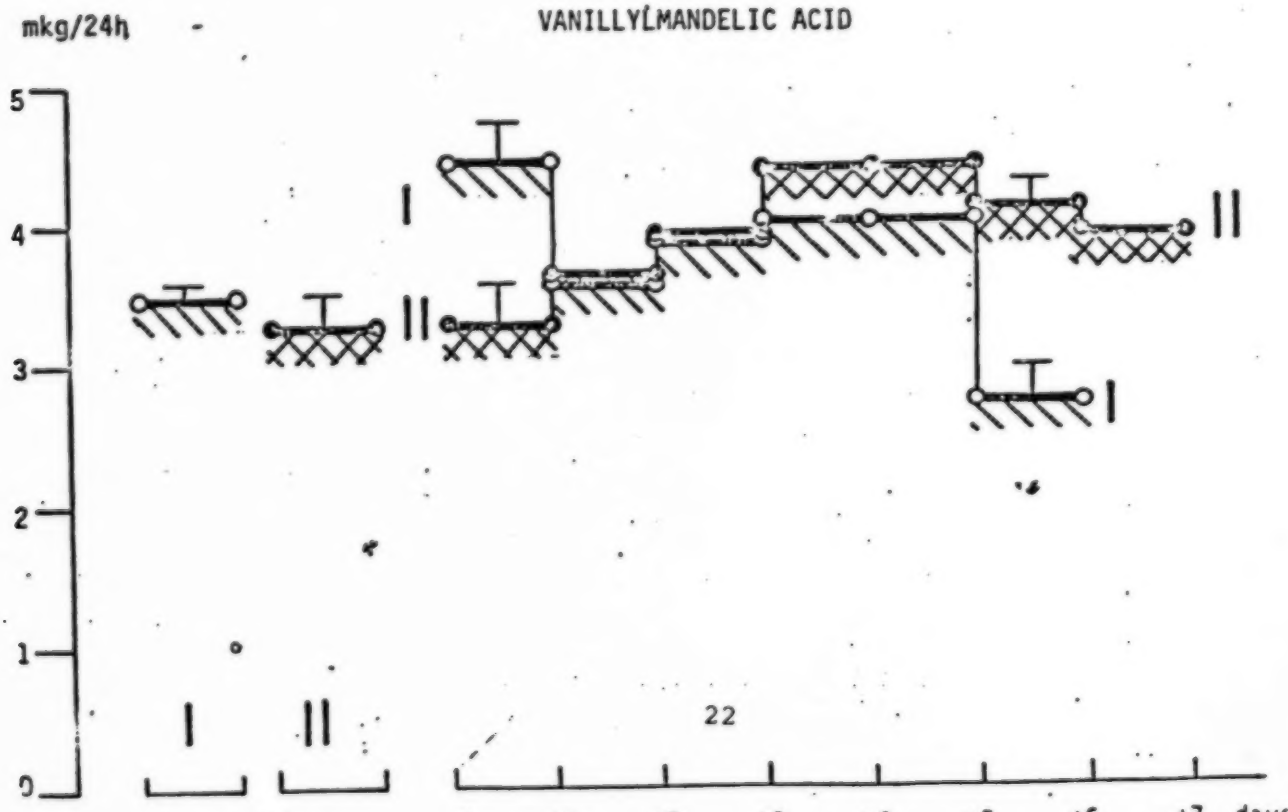

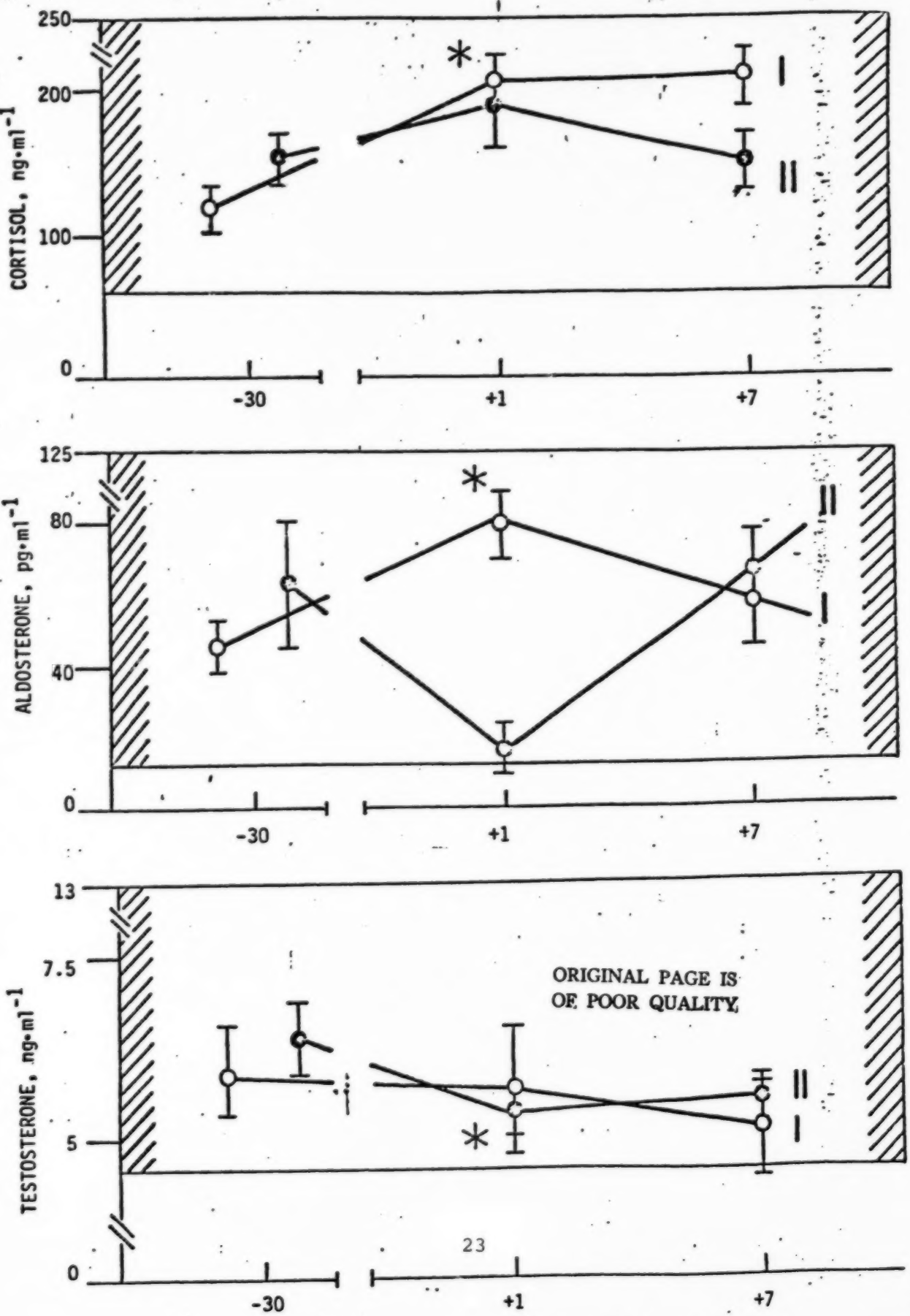

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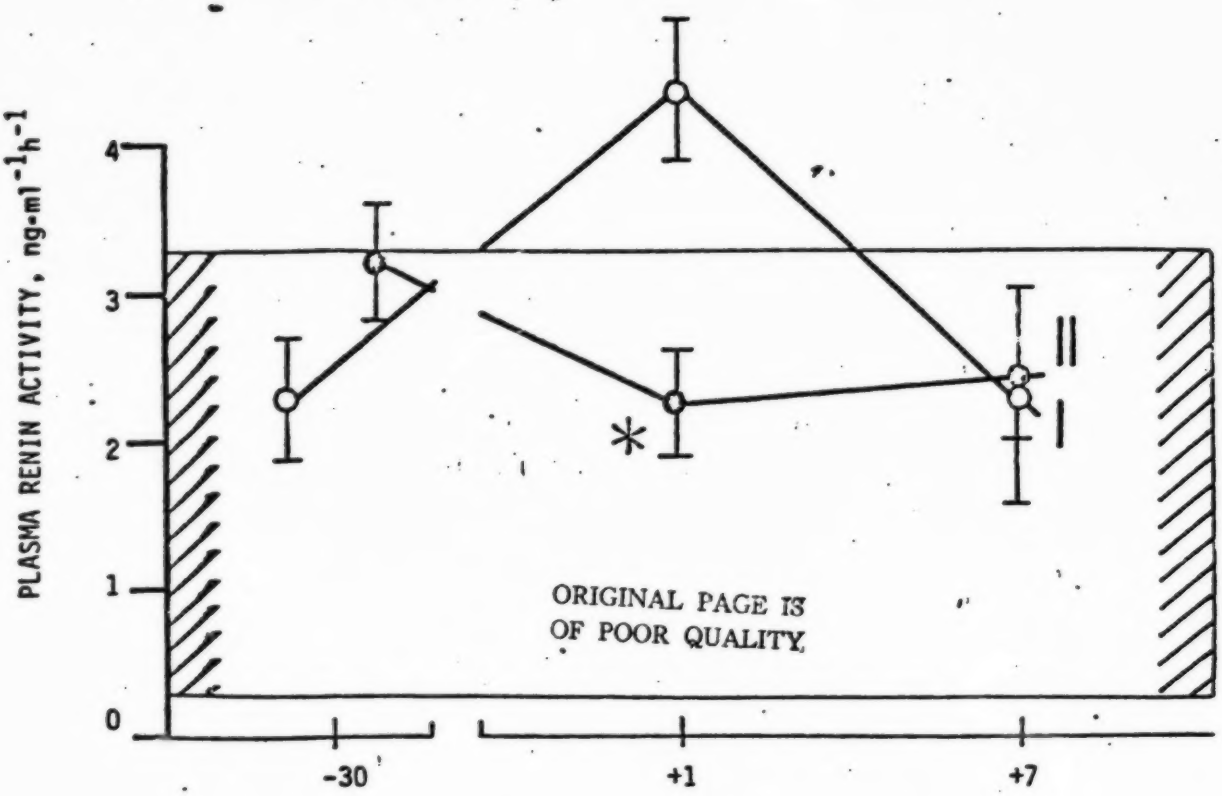
PLASMA RENIN ACTIVITY, RENAL EXCRETION OF ALDOSTERONE AFTER SHORT-TERM (I,n=15) AND LONG-TERM (II,n=9) SPACE FLIGHTS

21



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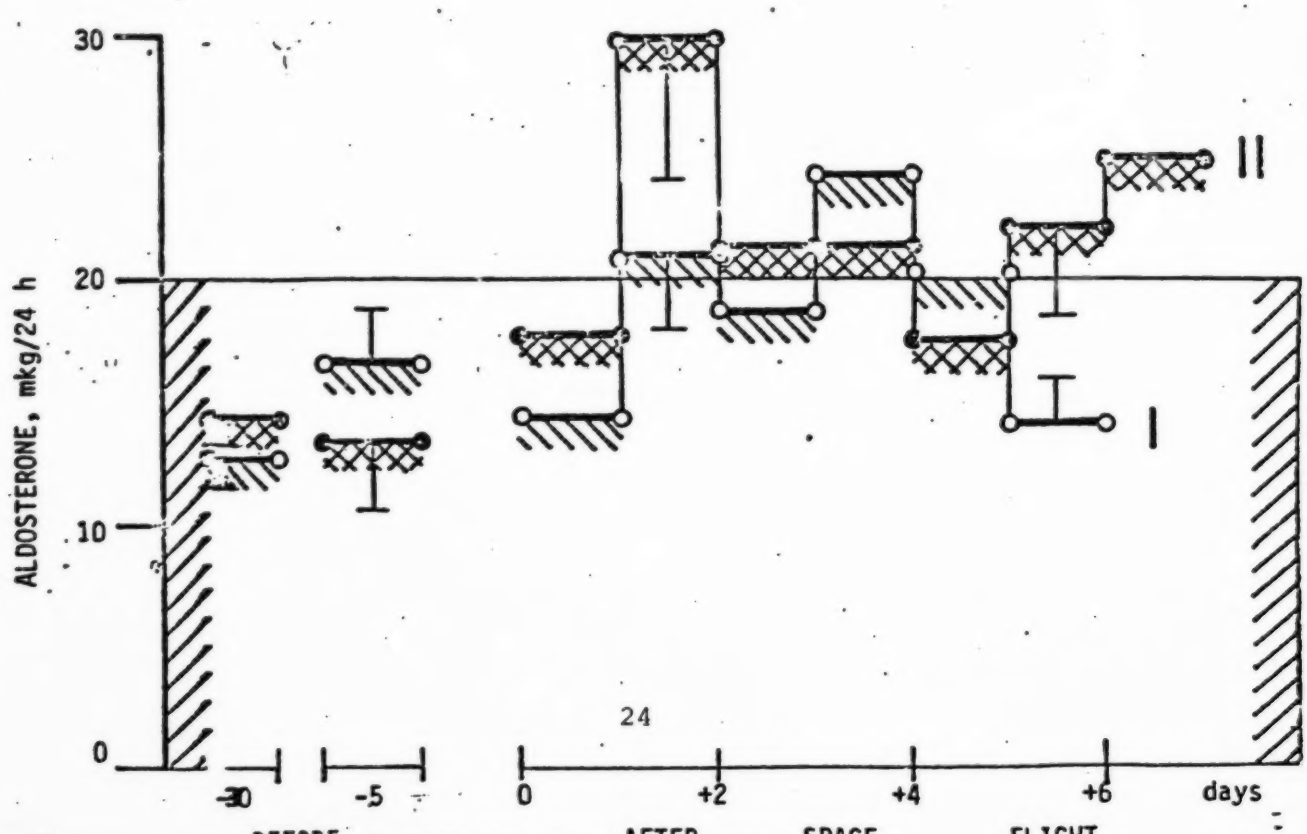
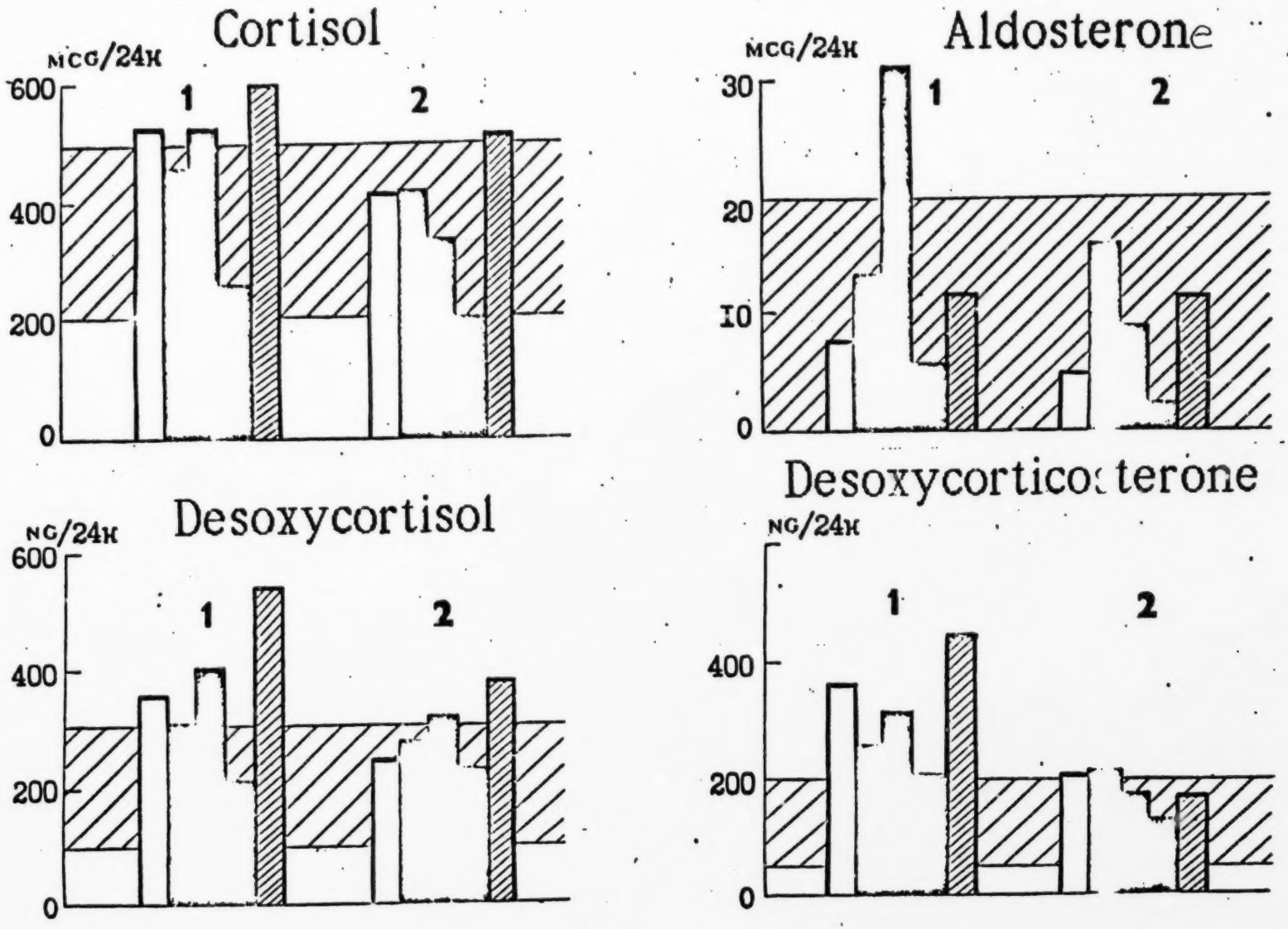
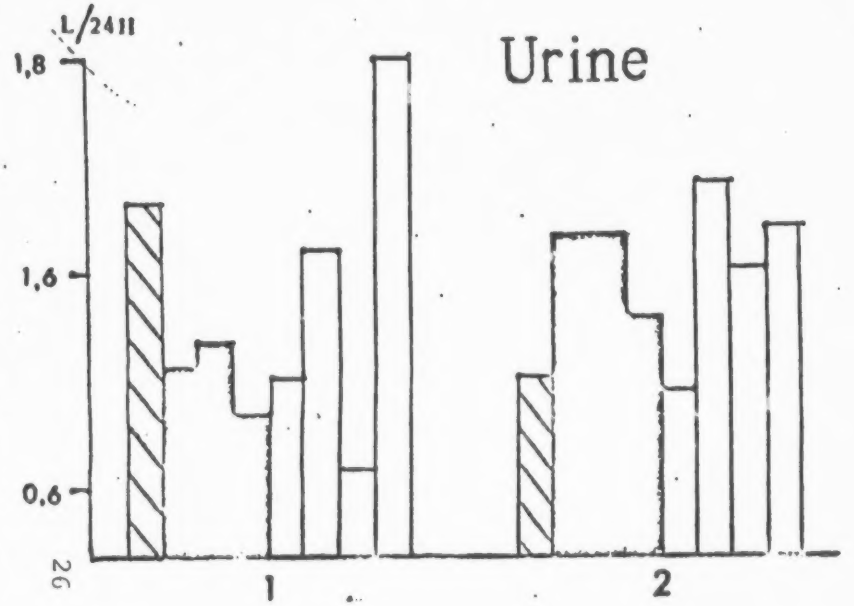
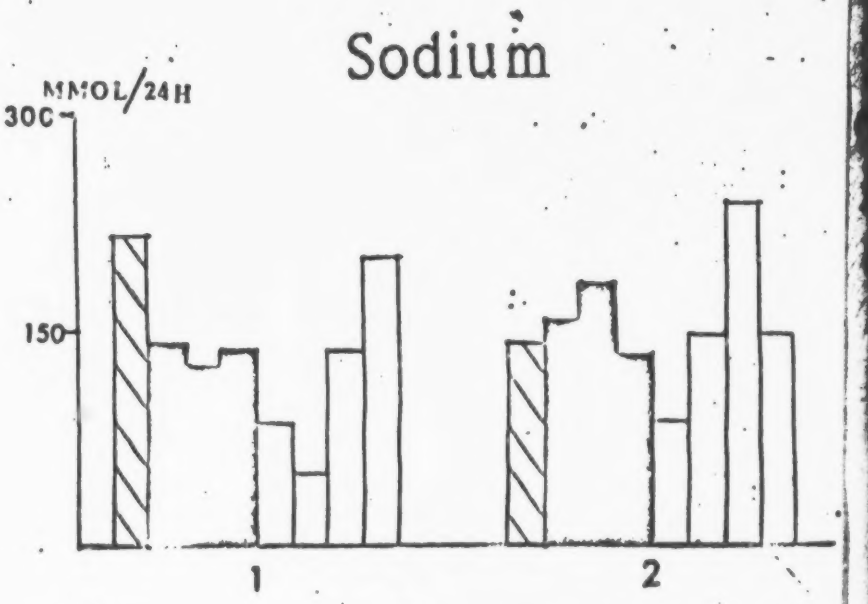
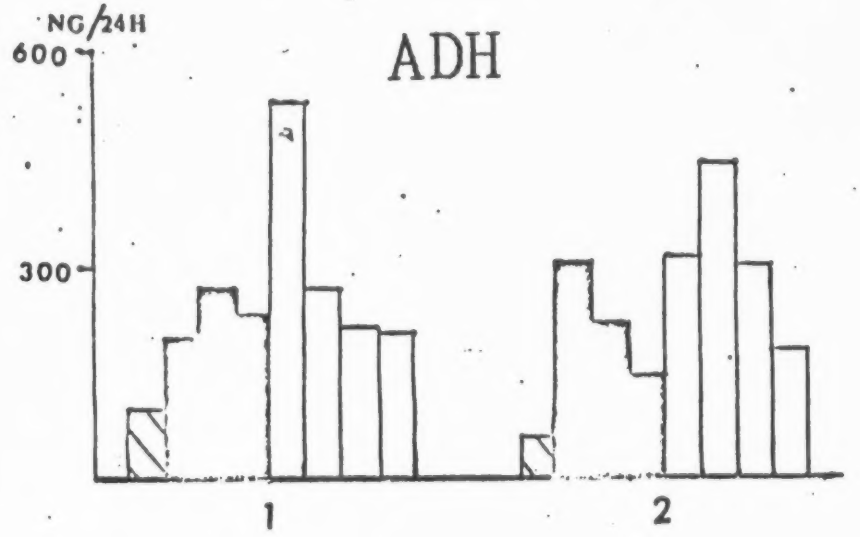
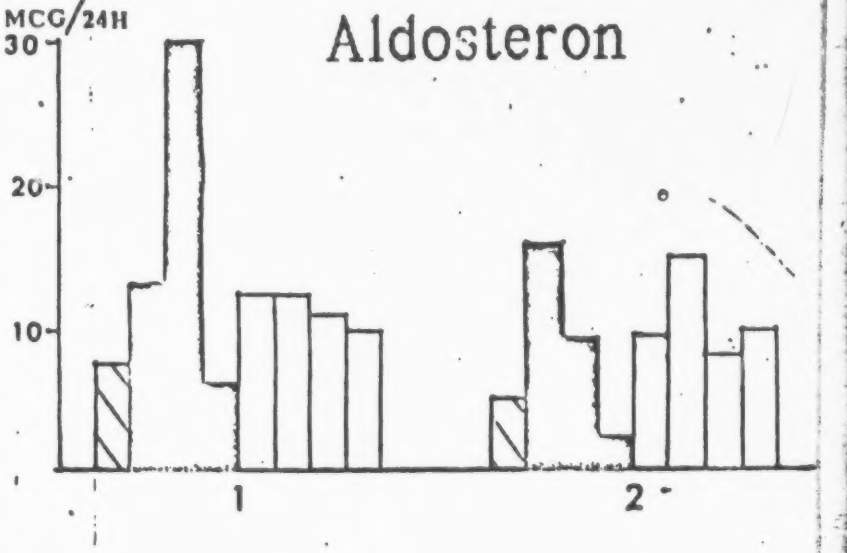



Cortisol
MCG/24H
600
400
200
0
1
2
Aldosterone
MCG/24H
30
20
10
0
1
2
Desoxycortisol
NG/24H
600
400
200
0
1
2
Desoxycorticosterone
NG/24H
400
200
0
1
2
- MEANS FOF THREE PREFLIGHT DAYS
-217-219 DAYS INFLIGHT
- MEANS FOR THREE POSTFLIGHT DAYS

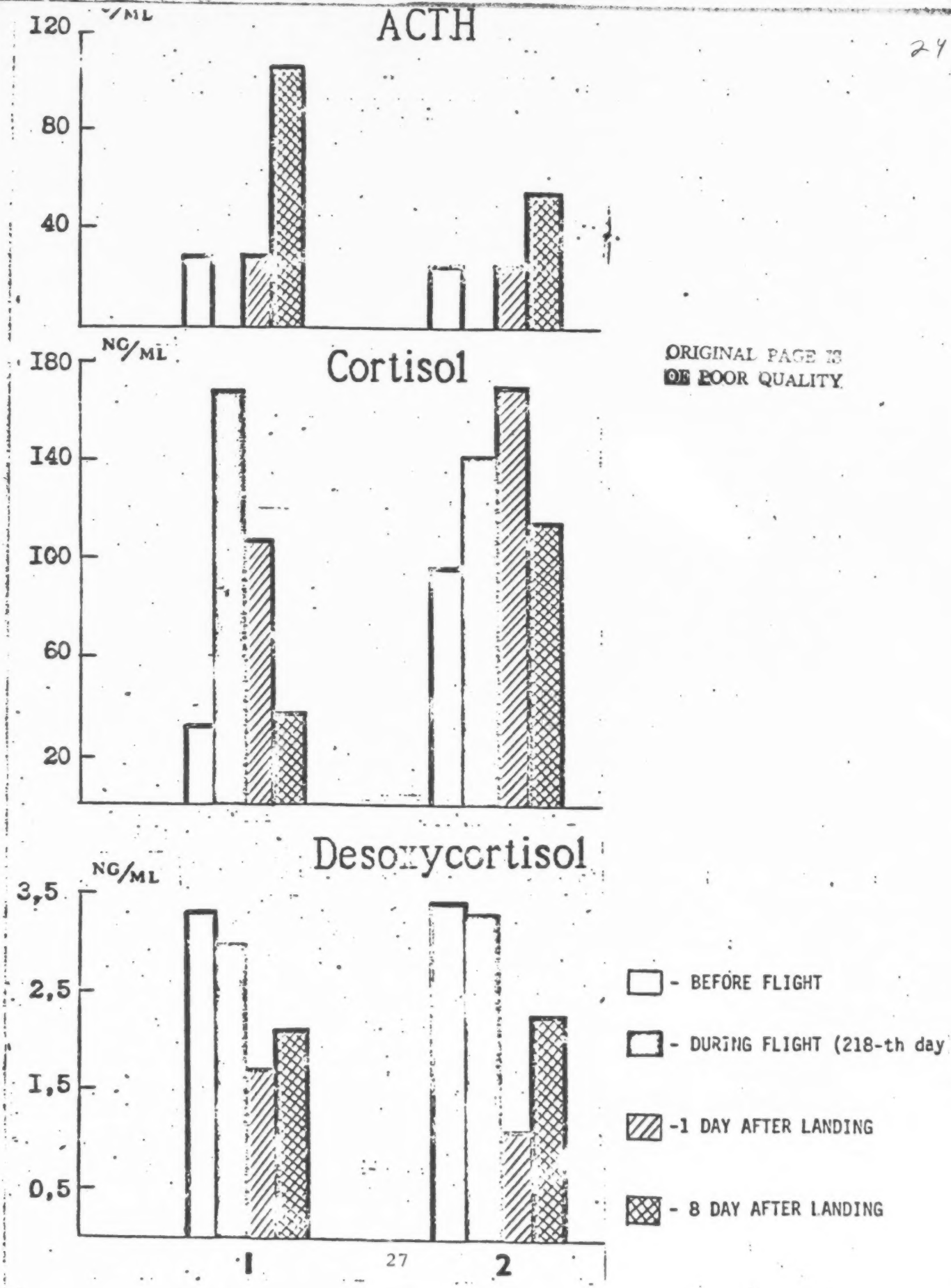








URINE FOR THREE PRECEDING DAYS — 2nd - 3rd DAYS INFUSION — FOUR DAYS PRECEDING



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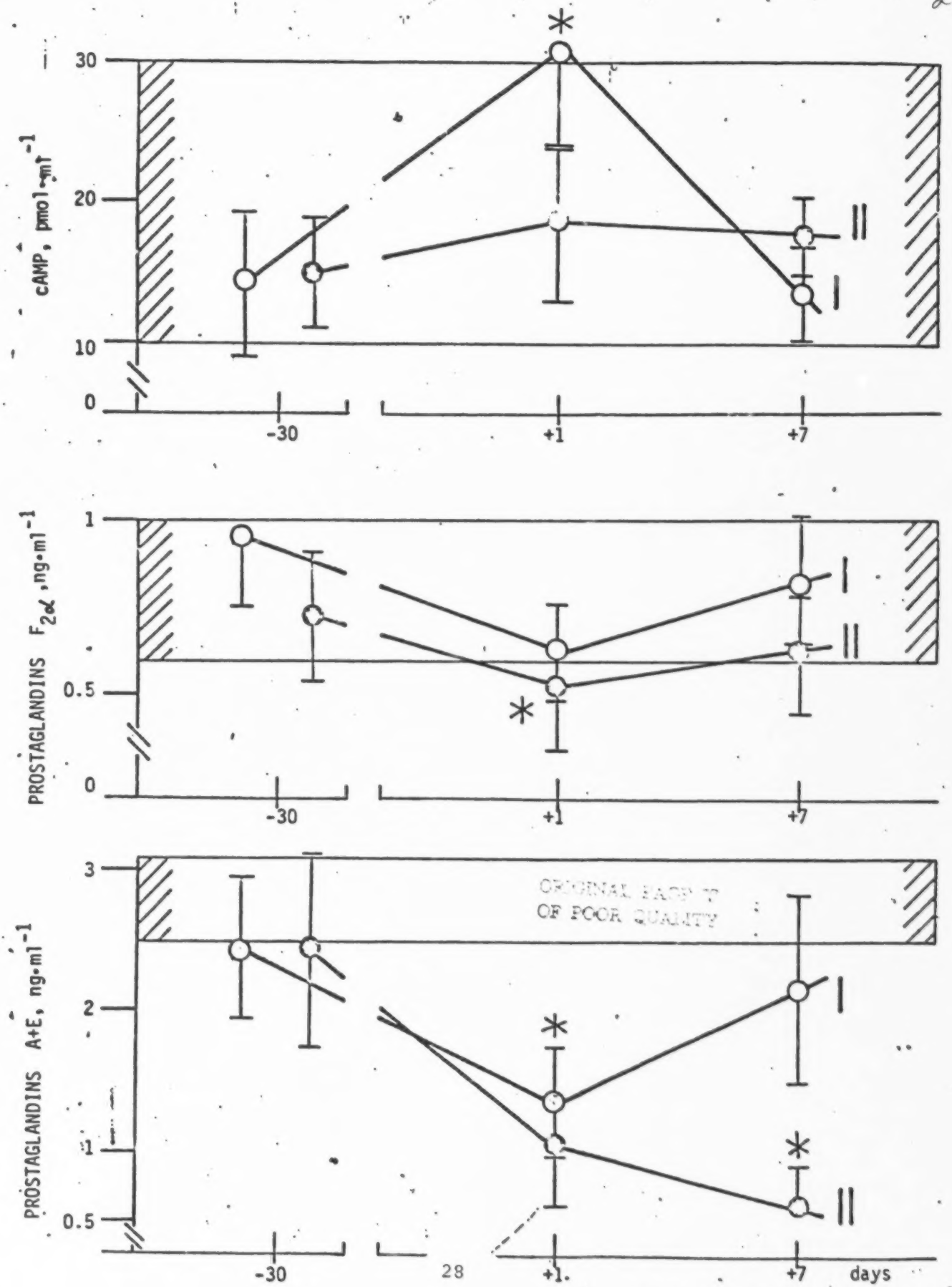
(I,n=10) AND LONG-TERM (II,n=10) SPACE FLIGHTS



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(I,n=17) AND LONG-TERM (II,n=10) SPACE FLIGHTS

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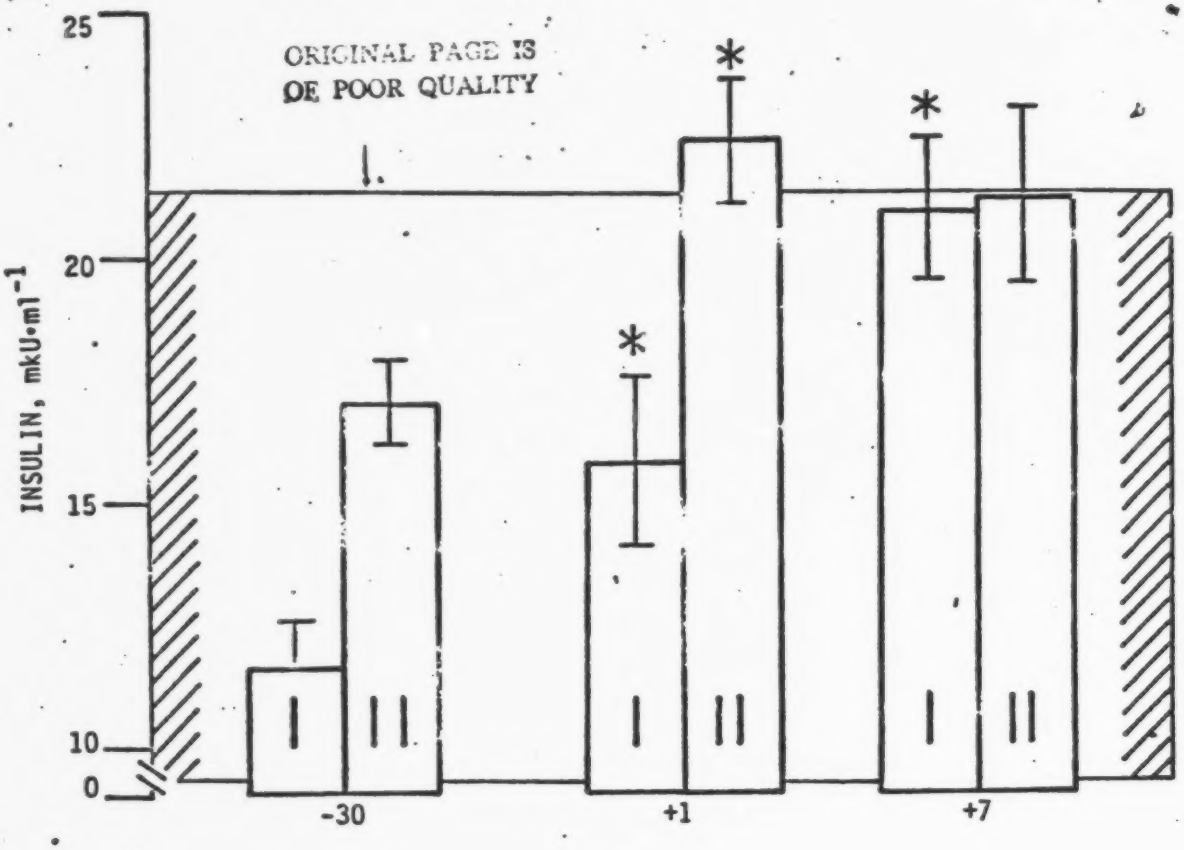
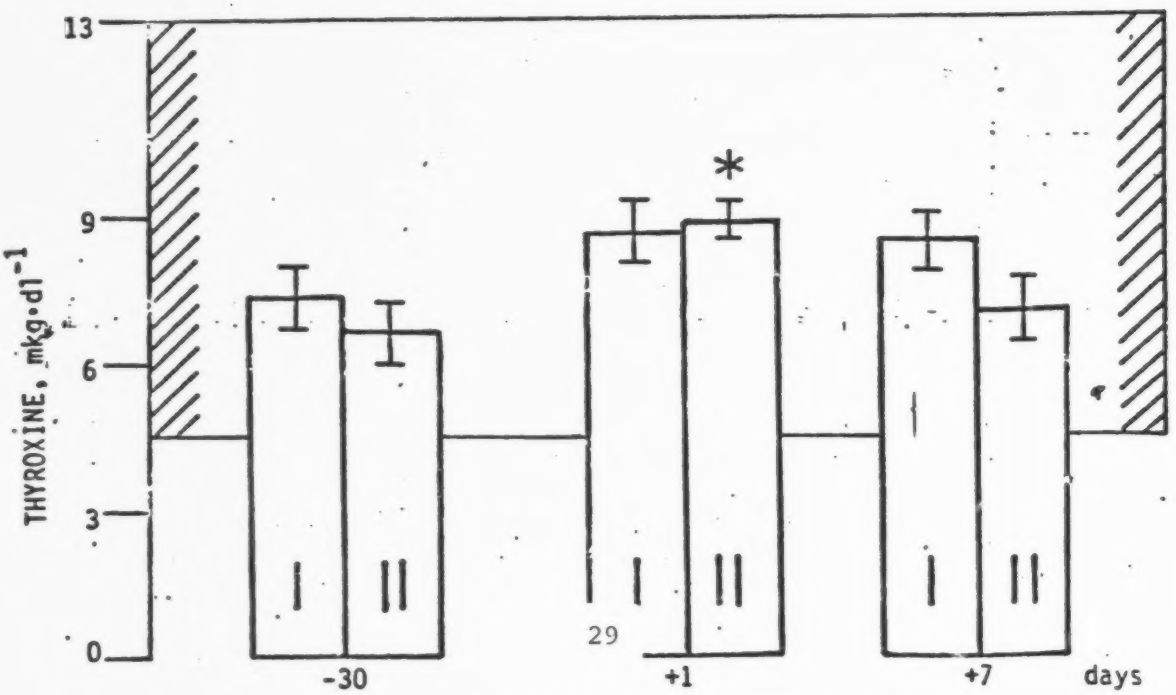
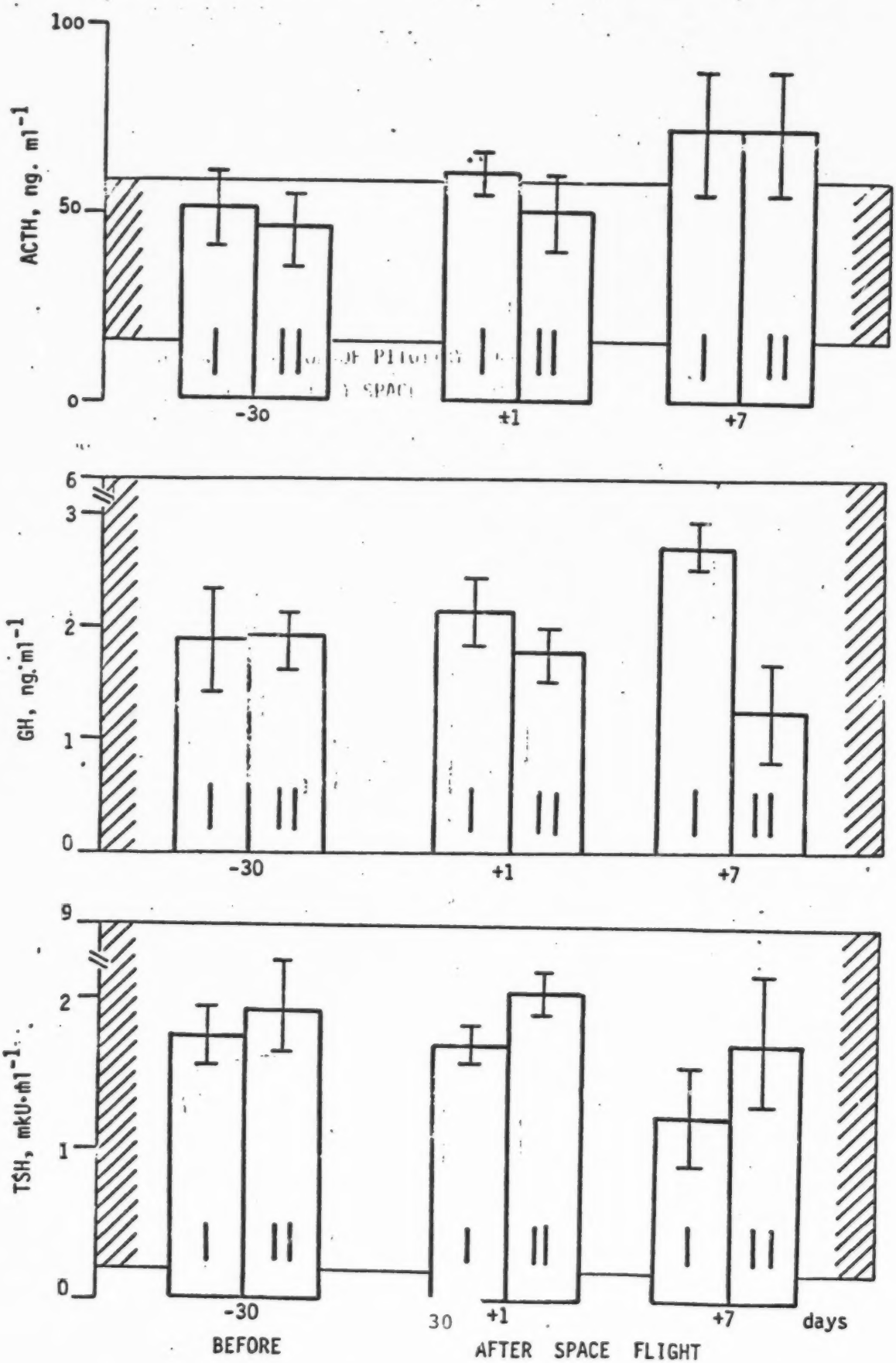




BLOOD CONCENTRATION OF PITUITRY HORMONES AFTER SHORT-TERM (I,n=17)
LONG-TERM (II,n=10) SPACE FLIGHTS



CHARACTERISTICS OF ENERGY PROCESS IN ERYTHROCYTES
BEFORE AND AFTER A 150-DAYS FLIGHT

	GLUC mcM/gHb/hour			LACTAT mcM/g Hb/hour			ATP mcM/gHb			2,3-DPG mcM/gHb			LDG mcM NADH/		
	BEFORE	R + 1	R + 7	BEFORE	R + 1	R + 7	BEFORE	R + 1	R + 7	BEFORE	R + 1	R + 7	BEFORE	R + 1	R
1	4,30	4,36	3,83	8,61	7,33	7,25	4,90	3,25	4,92	13,40	16,22	_	25,82	31,03	
2	3,20	2,49	3,05	8.88	5,40	6,42	5,89	3,08	4,80	14,22	16,22	13,86	25,57	30,63	2

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CHARACTERISTICS OF OXIDO-REDUCTIVE PROCESSES IN RED BLOOD CELLS
BEFORE AND AFTER A 150- DAYS FLIGHT

	G6P[illegible] mcM/g Hb			G6PD mcM $NADPH_2$/gHb			GSH mcM/g Hb			GSSG mcM/g Hb		
	BEFORE	R + 1	R + 7	BEFORE	R + 1	R + 7	BEFORE	R + 1	R + 7	BEFORE	R + 1	R + 7
1	191	130	97	4,12	5,19	-	6,91	5,48	6,10	20	60	120
2	117	99	138	3,39	5,95	3,13	9,62	8,70	6,69	26	42	102

CHARACTERISTICS OF ERYTHROCYTE MEMBRANES

BEFORE AND AFTER A 150-DAYS SPACE FLIGHT

	RATE OF K^+ RELEASE mcM/l rbc/hr			GSSG CONCENTRATION mM /l rbc oxidation stress			RATE OF HEMOLYSIS % min^{-1} MECHANICAL LOAD		
	BEFORE	R + 1	R + 7	BEFORE	R + 1	R + 7	BEFORE	R + 1	R + 7
1	2,0	1,5	1,2	300	270	350	1,2	1,4	2,6
2	1,2	1,1	1,2	350	410	450	1,2	0,9	1,8

CONTENT OF FATTY ACIDS OF TOTAL LIPIDS AND STATE OF LIPID PEROXIDATION IN ERYTHROCYTE MEMBRANES BEFORE AND AFTER 150- DAYS SPACE FLIGHT

PARAMETERS	PHYSIOLOGICAL norm	COSMONAUT 1			COSMONAUT 2		
FATTY ACIDS,%		BEFORE	R + 1	R + 7	BEFORE	R + 1	R + 7
MYRISTIC (14:0)	1,2 ± 0,1	-	1,6	0,9	-	0,8	0,7
PALMITIC (16:0)	23,8 ± 0,4	-	27,3	19,6	-	30,5	23,7
PALMITOOLEIC (16:1)	3,9 ± 0,3	-	4,9	2,4	-	4,9	5,2
HEXADECADIENIC(16:2)	1,6 ± 0,2	-	2,9	2,0	-	1,7	1,9
STEARIC (18:0)	20,7 ± 0,7	-	31,4	25,3	-	29,8	21,3
OLEIC (18:1)	23,5 ± 0,7	-	27,7	26,1	-	27,2	22,8
LINOLIC (18 :2)	10,5 ± 0,4	-	1,9	7,6	-	2,4	7,3
LINOLENIC (18:3)	1,9 ± 0,3	-	1,9	0,8	-	2,4	2,8
EICOSATRIENIC (20:3)	3,8 ± 0,3	-	-	3,4	-	-	5,1
ARACHIDONIC (20:4)	10,3 ± 1,0	-	-	11,4	-	-	6,8
LIPID PEROXIDATION PRODUCTS nA/mg lipids							
HYDROPEROXIDES	21,4 ± 0,4	46,87	20,59	-	24,1	22,7	27,55
END PRODUCTS	48,6 ± 4,6	131,70	48,90	-	57,6	42,61	80,54